Figures 21A-F show a schematic cross-sectional view of the synthesis of an addressable array, in accordance with Figures 19B-C.

Please replace the paragraph on page 24, lines 7-14 with the following paragraph:

The 1,000 different addresses can be unique capture oligonucleotide sequences (e.g., 24-mer) linked covalently to the target-specific sequence (e.g., approximately 20- to 25-mer) of a LDR oligonucleotide probe. A capture oligonucleotide probe sequence does not have any homology to either the target sequence or to other sequences on genomes which may be present in the sample. This oligonucleotide probe is then captured by its addressable array-specific portion, a sequence complementary to the capture oligonucleotide on the addressable solid support array. The concept is shown in two possible formats, for example, for detection of the p53 R248 mutation (Figures 13A-C).

Please replace the paragraph on page 24, line 15 to page 25, line 16 with the following paragraph:

In Figures 13A-C the top portion of the diagram shows two alternative formats for oligonucleotide probe design to identify the presence of a germ line mutation in codon 248 of the p53 tumor suppressor gene. The wild type sequence codes for arginine (R248), while the cancer mutation codes for tryptophan (R248W). The bottom part of the diagram is a schematic diagram of the capture oligonucleotide. The thick horizontal line depicts the membrane or solid surface containing the addressable array. The thin curved lines indicate a flexible linker arm. The thicker lines indicate a capture oligonucleotide sequence, attached to the solid surface in the C to N direction. For illustrative purposes, the capture oligonucleotides are drawn vertically, making the linker arm in section B appear "stretched". Since the arm is flexible, the capture oligonucleotide will be able to hybridize 5' to C and 3' to N in each case, as dictated by base pair complementarity. A similar orientation of oligonucleotide hybridization would be allowed if the oligonucleotides were attached to the membrane at the N-terminus. In this case, DNA/PNA hybridization would be in standard antiparallel 5' to 3' and 3' to 5'. Other modified sugar-phosphate backbones would be used in a similar fashion. Figure 13A shows two LDR primers that are designed to discriminate wild type and mutant p53 by containing the discriminating base C or T at the 3' end. In the presence of the correct target DNA and *Tth* ligase, the discriminating probe is covalently attached to a common downstream oligonucleotide. The downstream oligonucleotide is fluorescently labeled. The discriminating oligonucleotides are distinguished by the presence of unique addressable array-specific portions, Z1 and Z2, at each of their 5' ends. A black dot

indicates that target dependent ligation has taken place. After ligation, oligonucleotide probes may be captured by their complementary addressable array-specific portions at unique addresses on the array. Both ligated and unreacted oligonucleotide probes are captured by the oligonucleotide array. Unreacted fluorescently labeled common primers and target DNA are then washed away at a high temperature (approximately 65°C to 80°C) and low salt. Mutant signal is distinguished by detection of fluorescent signal at the capture oligonucleotide complementary to addressable array-specific portion Z1, while wild type signal appears at the capture oligonucleotide complementary to addressable array-specific portion Z2. Heterozygosity is indicated by equal signals at the capture oligonucleotides complementary to addressable array-specific portions Z1 and Z2. The signals may be quantified using a fluorescent imager. This format uses a unique address for each allele and may be preferred for achieving very accurate detection of low levels of signal (30 to 100 attomoles of LDR product). Figures 13B-C shows the discriminating signals may be quantified using a fluorescent imager. This format uses a unique address where oligonucleotide probes are distinguished by having different fluorescent groups, F1 and F2, on their 5' end. Either oligonucleotide probe may be ligated to a common downstream oligonucleotide probe containing an addressable array-specific portion Z1 on its 3' end. In this format, both wild type and mutant LDR products are captured at the same address on the array, and are distinguished by their different fluorescence. This format allows for a more efficient use of the array and may be preferred when trying to detect hundreds of potential germline mutations.

Please replace the paragraph at page 45, line 21 to page 46, line 2 with the following paragraph:

Figures 21A-F show a schematic cross-sectional view of the synthesis of an addressable array (legend). Figure 21A shows attachment of a flexible spacer (linker) to surface of array. Figure 21B shows the synthesis of the first rows of oligonucleotide tetramers. Only the first row, containing tetramer 1, is visible. A multi-chamber device is placed so that additional rows, each containing a different tetramer, are behind the first row. Figure 21C shows the synthesis of the first columns of oligonucleotide tetramers. The multi-chamber device or surface has been rotated 90°. Tetramers 9, 18, 7, and 12 were added in adjacent chambers. Figure 21D shows the second round synthesis of the oligonucleotide rows. The first row contains tetramer 2. Figure 21E shows the second round of synthesis of oligonucleotides. Tetramers 34, 11, 14, and 23 are added in adjacent chambers during the second round. Figure 21F shows the third round synthesis of PNA rows. The first row contains tetramer 3. Figure 21F shows the structure of the array after third round synthesis of columns, adding tetramers 16, 7, 20, 29. Note that all 24-mer oligonucleotides within a given row or column are unique, hence achieving the desired addressable array. Since each 24-mer

differs from its neighbor by three tetramers, and tetramers differ from each other by at least 2 bases, then each 24-mer differs from the next by at least 6 bases. Each mismatch significantly lowers T_m, and the presence of 6 mismatches in just 24 bases would make cross hybridization unlikely even at 35°C. Note that the smaller 12-mer sequences are identical with one another, but are not at all common with the 24-mer sequences. Even though the particular 12-mer sequence may be found within a 24-mer elsewhere on the grid, for example 17-1-2-3-28-5, an oligonucleotide will not hybridize to the 12-mer at temperatures above 50°C.